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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/555,108	07/21/00	CHARMAN	S 13627

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EXAMINER

HOLLERAN, A

ART UNIT	PAPER NUMBER
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1642

DATE MAILED:

05/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

# Office Action Summary

Application No.

09/555,108

Applicant(s)

Charman et al

Examiner

Anne Holleran

Art Unit

1642



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_\_.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-43 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☒ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6 20) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

1. The Preliminary Amendment, filed May 24, 2000, is acknowledged.

Claim 43 was added.

2. Claims 1-43 are pending and examined on the merits.

### *Claim Rejections - 35 USC § 112*

3. Claims 1-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

*main fair*  
*pg. 4 missing* Claims 1, 6, 21, and 33 are indefinite because the claims are drawn to derivatives or homologues of LIF. The scope of the claims cannot be determined because it is not clear what chemical structures are encompassed by derivatives or homologues of LIF.

*main fair* Claim 6 is indefinite because it is drawn to compositions comprising functional equivalents of a surfactant. The scope of the claim is not clear because the term "surfactant" already defines a group of compounds by a function. Thus, it is not clear why it is necessary to include the phrase "functional equivalent thereof".

Claim 7 is indefinite because it is drawn to a composition comprising a "buffer species".  
The scope of the claim is not clear because it is unclear what chemical compounds are

encompassed by the term "buffer species". The specification does not provide a closed definition of what compounds are encompassed by the term "buffer species".

Claim 7 is indefinite because it is drawn to a composition comprising a "polymeric compound". The scope of the claim is not clear because it is unclear what chemical compounds are encompassed by a "polymeric compound". The specification does not provide a closed definition of what compounds are encompassed by the term "polymeric".

Claims 11, 27 and 38 are indefinite because they are drawn to compositions or methods comprising a "polyoxyethylene derivative". The scope of the claim is not clear because it is unclear what chemical compounds are encompassed by a "polyoxyethylene derivative". A derivative may be a part of a compound or may be a compound with an additional chemical moiety.

Claims 33-42 are drawn to the use of stabilizing agents. However, the claims do not set forth any steps involved in a method or process, and it is unclear what method or process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 33-42 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

4. Claims 1-3, 6-13, 15, 16, 20-29, 32-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Patterson et al (U.S. 6,156,729; issued Dec. 5, 2000; filed Oct. 15, 1997) as evidenced by Cleland et al (Cleland, J.L. et al. Crit. Rev. Therapeutic Drug Carrier Systems 10: 307-377, 1993).

Claims 1 and 6-13 are drawn to compositions of LIF and a stabilizing agent. The stabilizing agent may be an isotonicity agent, an agent which increases or maintains the conformational stability of LIF or a surfactant. The isotonicity agent may be a polyhydric alcohol, a buffer, a sugar or a pharmaceutically acceptable polymer. The polyhydric alcohol may be sorbitol. The surfactant may be anionic, cationic, amphoteric or non-ionic. The surfactant may be a fatty alcohol, a glyceryl ester or a fatty acid ester of either a fatty alcohol or other alcohol. The stabilizing agent may be a polysorbate, a polyoxyethylene, or a polyoxyethylene polyoxypropylene copolymer. The buffer may be phosphate a citrate or an acetate buffer. The composition may contain LIF in an amount from 0.1 ug/ml to 100 mg/ml. Claim 2 is drawn to a composition of claim 1 wherein the stabilizing agent facilitates reduced aggregation of LIF. Claim

3 is drawn to a composition of claim 1 wherein the stabilizing agent facilitates reduced deamidation of LIF. Claim 15 is drawn to a composition of claim 6 wherein the aggregation of LIF over time is reduced. Claim 16 is drawn to a composition of claim 6 wherein the deamidation of LIF over time is reduced.

Claims 21-29 and 32 are drawn to methods of preparing a composition comprising LIF, comprising admixing LIF with a stabilizing agent.

Claims 33-40 are drawn to uses of a stabilizing agent. These claims may be interpreted as either a method claim or a product claim. In the case of a method claim, for the purposes of examination, claims 33-40 are interpreted as drawn to methods of preparing a composition comprising LIF, comprising admixing LIF with a stabilizing agent. In the case of a composition claim, claims 33-40 are interpreted as drawn to compositions comprising LIF and a stabilizing agent.

Patterson teaches pharmaceutical compositions of LIF and stabilizing agent (see column 4, lines 65-column 5, line 12). The stabilizing agent may be a phosphate or citrate buffer; glucose, mannose or dextrose (sugars); mannitol or sorbitol (polyhydric alcohols); Tween, Pluronic, PEG (non-ionic surfactants; PEG is a polymer; Pluronic is a polyoxyethylene polyoxypropylene copolymer; Tween is a fatty acid ester and comprises a polyoxyethylene moiety).

Surfactants are known (as evidenced by Cleland, page 320) to decrease aggregation of proteins. Buffers which maintain a pH below 6 are known to decrease deamidation (as evidenced by Cleland, pages 328-333 and 337). Citrate buffer is a buffer that would maintain a pH below 6.

Patterson teaches LIF at concentration of 100 or 1000 ng/ml (same as 0.1 ug/ml and 1ug/ml).

Thus, Patterson teaches compositions comprising LIF that are the same as that claimed.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 4, 5, 14, 17-19, 30, 31 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patterson (*supra*) in view of Cleland (*supra*).

Claims 4, 5, 14, 17-19, 30, 31 and 43 include the limitation that the pH of the composition be between 3.5 and 6.5 or 4.5 and 5.5. Patterson fails to teach an optimal pH for compositions of LIF. However, an examination of the amino acid sequence of LIF shows that LIF has many asparagine and glutamine residues and would thus be susceptible to degradation by deamidation. Cleland teaches the mechanisms by which deamidation reactions occur and teaches that pH is a characteristic of a formulation that may be controlled to reduce deamidation reactions. Cleland also suggests that a pH below 6 would be optimal for many proteins (see pages 328-333 and 337). Thus, it would have been *prima facie* obvious to one of skill in the art at the time the

invention was made to have found the optimal pH of LIF which would decrease deamidation degradation.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.



Anne L. Holleran  
Patent Examiner  
May 5, 2001



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